REMARKS

Reconsideration of the application in view of the above amendments and following remarks is requested. Claims 89, 102-111 are currently being examined. Claims 105, 106, 110, and 111 have been amended. Entry of this amendment is respectfully requested as it places the present application in better form for appeal. It is believed that the present amendments and arguments should put this application in condition for allowance. However, in order to preserve the rights of Applicants, a Notice of Appeal is being filed concurrently herewith.

Claims 105, 106, 110, and 111 have been amended to alternatively describe the multimeric proteins of the claims. Support for this amendment in the specification is at least at page 45, lines 24-27, where the specification discloses the use of one or more polypeptide fusions in a multimeric protein.

A. Rejection Under 35 U.S.C. § 112, second paragraph

Claims 82 and 94 are rejected as allegedly vague by the use of the phrase "the composition comprises multimeric proteins comprising one or more fusion proteins." The claims have been amended to recite "multimeric proteins" (or dimeric) and "polypeptide fusions" in order to clarify that one or more species of polypeptide fusions can comprise a multimeric (or dimeric) protein.

B. Provisional Rejection of Claims 89, 102-111 for Double Patenting

Claims 89, 102-111 have been provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over Claims 64-96 of copending Application No. 09/569,245. In order to speed prosecution, Applicants enclose a terminal disclaimer for this application as the two are commonly owned. The provisional rejection is therefore overcome.

C. Rejection Under 35 U.S.C. §§ 102(a) and (b)

Claims 89, 102 and 107 have been rejected under 35 U.S.C. § 102(a) as being anticipated by Bram et al. (WO 98/39361) and under 35 U.S.C. § 102(e) as being anticipated by Bram et al. (U.S. Patent 5,696,102). Applicants continue to respectfully traverse these rejections.

The Examiner bases his rejections on the disclosure in both the Bram et al. references of a composition "identical to those of the instant invention" and the possession of that composition of "the same properties as those of the instant invention (including the ability to bind the ztnf4)" (Final Rejection of 4/28/03, page 4). However, the present invention must be defined in terms of the claim language. The pending claims are not to a composition but to methods of use, specifically, methods of inhibiting B lymphocyte proliferation in a mammal wherein the soluble

receptor binds the ztnf4 protein. To anticipate the specifically claimed method, there must be disclosure by Bram et al. of each limitation of the present claim, including the binding of the ztnf4 protein to the soluble receptor. But the binding cannot be disclosed in the Bram et al. reference as neither the existence of the ztnf4 protein nor the ligand-receptor relationship between ztnf4 and TACI were known at the time of the publication of this reference. Indeed, the Bram et al. reference states at page 52, line 19 that the endogenous ligand of the TACI protein is unknown. Only through the present disclosure is the identity of ztnf4 as the ligand for the TACI receptor made, and only through impermissible hindsight reconstruction of this information with the disclosure of Bram et al. could the presently claimed method be characterized as anticipated.

The Examiner appears to be stating that the presently claimed method of inhibiting B lymphocyte proliferation and the binding of ztnf4 is inherently disclosed in the Bram et al. reference. Applicants strongly disagree with this interpretation of the reference's teachings. Disclosure of a receptor does not inherently disclose the identity of its ligand nor the ligand's ability to cause B lymphocyte proliferation, a statement that is particularly true when the ligand protein is unknown when the receptor is disclosed, as is the case with the TACI receptor and ztnf4. It is respectfully submitted that it would have required undue experimentation to determine that the proliferation of B lymphocytes caused by ztnf4 is inhibited through the administration of the recited TACI fusion proteins at the time of the Bram et al. publication. This standard for the determination of inherent teachings was very recently restated and clarified by the Federal Circuit in Elan Pharmaceuticals v. Mayo Foundation for Med. Educ. and Research, 2003 U.S. App. LEXIS 20195 (October 2, 2003). There the court stated that "anticipation requires that the assertedly anticipating disclosure enabled the subject matter of the reference and thus of the patented invention without undue experimentation." Id. at *2.

The conclusion of undue experimentation in this case is supported by the significant amount of experimentation that would be required in addition to the Bram et al. teachings to reach the present method. It would be necessary to (1) isolate an unknown protein, (2) identify its ability to cause B lymphocyte proliferation, and (3) determine that this activity is inhibited by the administration of TACI fusion proteins, and (4) determine that the protein and TACI bind. Additionally, all this must occur in the relatively unpredictable biotechnology art. In light of this amount of experimentation, the claimed methods are not enabled so cannot be inherently disclosed by the teachings of Bram et al. The rejection of the claims as anticipated based on this reference should therefore be withdrawn.

D. Rejection Under 35 U.S.C. § 103(a)

Claims 89, 102-111 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Bram et al. (WO 98/39361), as cited above, in view of Presta et al. (U.S. Patent No. 5,739,277). Applicants respectfully traverse this rejection.

As discussed extensively above, the Bram et al. disclosure does not expressly nor inherently teach the ztnf4 protein, its activities, or the ability of TACI and ztnf4 to bind, all central aspects of the currently claimed method of use. Presta et al., cited by the Examiner to provide the teaching of the use of IgG1 as the source of the Fc portion of an immunoglobulin fusion protein, does not remedy these deficiencies. Since the combination of references fails to teach all limitations of the presently claimed method, this rejection does not render obvious the presently claimed method and is properly withdrawn.

On the basis of the above amendments and remarks, Applicants believe that each rejection has been addressed and overcome. Reconsideration of the application and its allowance are requested. If for any reason the Examiner feels that a telephone conference would expedite prosecution of the application, the Examiner is invited to telephone the undersigned at (206) 442-6627.

Respectfully Submitted,

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Enclosures:

Petition and Fee for Extension of Time (in duplicate)
Notice of Appeal
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